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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/562,296 | 12/22/2005 | Peter William Gage | 64681(70403) | 3685 |
| 21874 | 7590 | 04/19/2010 | EXAMINER | |
| EDWARDS ANGELL PALMER & DODGE LLP | | | CHANDRAKUMAR, NIZAL S | |
| P.O. BOX 55874 | | | ART UNIT | PAPER NUMBER |
| BOSTON, MA 02205 | | | 1625 | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/562,296 | GAGE ET AL. | |
| | Examiner | Art Unit | |
| | NIZAL S. CHANDRAKUMAR | 1625 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 12 February 2010.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-169 is/are pending in the application.
 4a) Of the above claim(s) 3-160 and 164-168 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1,2,161-163 and 169 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>11/02/2009</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Applicants response filed 02/12/2010 is acknowledged.

Claim status:

Claims 1 and 161 are amended. Claim 169 is new.

Claims 1-169 are in the application.

Claims 1, 2, 161-163, and 169 are under prosecution, while 3-160 and 164-168 are withdrawn.

Response to Remarks:

Claim Rejections - 35 USC § 112

Previously presented rejection is withdrawn in view of amendments to claims and applicants persuasive arguments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Previously presented rejection of claims 1, 161, 169 (new claim) and (dependent claims 2, 162, 163) rejected under 35 U.S.C. 103(a) as obvious is maintained for reasons of record.

Rejection over Yamamoto et al. Chemical & Pharmaceutical Bulletin (1997), 45(8), 1282-1286.

Applicant's arguments were fully considered but are not persuasive.

Applicant's arguments center on the following:

1. The issue is whether there is an apparent reason to combine the known elements in the fashion claimed by the patent at issue.
2. The issue is whether or not there is a reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.
3. The amended claims do not have the compounds disclosed by Yamamoto.

Further Yamamoto does not provide suggestion for (instantly claimed) modification.

Response:

The claimed compounds represent a) positional isomer and b adjacent homolog of the cited Yamamoto compounds.

a) Positional isomers, having the same radical on different positions of the molecule, are prima facie obvious, and require no secondary teaching. The experienced Ph.D. synthetic organic chemist, who would make Applicants' compounds, would be motivated to prepare these position isomers based on the expectation that such close analogues would have similar properties and upon the routine nature of such position isomer experimentation in the art of medicinal chemistry. It would be routine for the chemist to vary the point of attachment in order to increase potency and to establish

better patent protection for her compounds. In re JONES 74 USPQ 152 (4-methyl naphthyl-1-acetic acid and 2-methyl naphthyl-1-acetic acid obvious over a reference teaching 1-methyl naphthyl-2-acetic acid), quoted with approval by Ex parte MOWRY AND SEYMOUR 91 USPQ 219, Ex parte Ulliyot 103 USPQ 185 (4-hydroxy-1-oxo-1,2,3,4-tetrahydroisoquinoline obvious over a reference teaching 4-hydroxy-2-oxo-1,2,3,4-tetrahydroquinoline), "[p]osition isomers are recognized by chemists as similar materials", Ex parte BIEL 124 USPQ 109 (N-ethyl-3-piperidyl diphenylacetate obvious over a reference teaching N-alkyl-4-piperidyl diphenylacetate), "[appellant's arguments] do not, in any way, obviate the plain fact that appellant's DACTIL is an isomer of McElvain et al.'s compound. This close relationship places a burden on appellant to show some unobvious or unexpected beneficial properties in his compound in order to establish patentability", Ex parte Henkel 130 USPQ 474, (1-phenyl-3-methyl-4-hydroxypyrazole obvious over reference teaching 3-phenyl-5-methyl-4-hydroxypyrazole), "appellants have made no comparative showing here establishing the distinguishing characteristics they allege which we might consider as evidence that the claimed compounds are unobvious. It is clear from In re Henze, supra, and the authorities it cites, that at least this much is necessary to establish patentability in adjacent homologs and position isomers (emphasis added)". In re Surrey 138 USPQ 67, (2,6-dimethylphenyl-N-(3-dimethylaminopropyl) carbamate obvious over a reference teaching 2,4-dimethylphenyl N-(3-dimethylaminopropyl) carbamate), In re MEHTA 146 USPQ 284, (2-(1-methyl)-pyrrolidylmethyl benzilate obvious over a reference teaching 3-(1-methyl)-pyrrolidylmethyl benzilate), "[t]he fact that a position isomer (emphasis

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added) of a compound is known is some evidence of the obviousness of that compound. Position isomerism (emphasis added) is a fact of close structural (emphasis in original) similarity ... ". Deutsche Gold-Und Silber-Scheideanstalt Vormals Roessler v. Commissioner of Patents, 148 USPQ 412, (1-azaphenothiazines obvious over references teaching 2-azaphenothiazines, 3-azaphenothiazines, and 4-azaphenothiazines), In re Crounse, 150 USPQ 554 (dye with para (CONH₂) and ortho (OCH₃) obvious over a dye with the same nucleus and meta (CONH₂) and para (OCH₃) group), Ex parte Allais, 152 USPQ 66, (3- -aminopropyl-6-methoxyindole obvious over a reference teaching 3- -aminopropyl-5-methoxyindole), In re Wiechert 152 USPQ 247, (1-methyl dihydrotestosterones obvious over a reference teaching 2-methyl dihydrotestosterones), Monsanto Company v. Rohm and Haas Company, 164 USPQ 556, at 559, (3',4'-dichloropropionanilide obvious over references teaching 2',4'-dichloropropionanilide and 2',5'-dichloropropionanilide), Ex parte Naito and Nakagawa, 168 USPQ 437, (3-phenyl-5-alkyl-isothiazole-4-carboxylic acid obvious over a reference teaching 5-phenyl-3-alkyl-isothiazole-4-carboxylic acid), "[t]his merely involves position isomers (emphasis added) and under the decisions cited, the examiner's holding of *prima facie* obviousness is warranted." In re Fouche, 169 USPQ 429, (10-aliphatic substituted derivatives of dibenzo[a,d]cycloheptadiene obvious over reference teaching 5-aliphatic substituted derivatives of dibenzo[a,d]cycloheptadiene). Ex parte Engelhardt, 208 USPQ 343 at 349, "[i]f functional groups capable of withdrawing or repelling electrons are located in the chain or ring (emphasis added) of a biologically active compound, transfer of such groups to other positions in which their electronic

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effects are lessened or enhanced may alter the biological activity of the modified compound. Hence, position isomerism (emphasis added) has been used as a tool to obtain new and useful drugs", In re Grabiak 226 USPQ 870, "[w]hen chemical compounds have "very close" structural similarities and similar utilities, without more a *prima facie* case may be made", In re Deuel 34 USPQ2d 1210, "a known compound may suggest its analogs or isomers, either geometric isomers (cis v. trans) or position isomers (emphasis added) (e.g. ortho v. para)".

b) Adjacent homologs: Applicant's amendment claim to overcome anticipatory compounds. Thus applicants amend to remove methoxy substituent while retaining ethoxy substituent (see claim 1, numbered page 4, definition of variable Rj. Such adjacent homologs (methyl and ethyl) are obvious variants as they are suggestive of one another, and to one of skill in the art, no secondary teaching is needed.

Rejection over Bream, Arzneimittel-Forschung (1975), 25(10), 1477-82:

Applicant's arguments center on the following:

1. The differences between the compounds of this application and those of Bream include *different* substituents at *different* positions even for one portion (that is, the R1 moiety) out of the whole compound structure.

2. Bream does not provide suggestion for (instantly claimed) modification.

Applicant's arguments are not persuasive.

Response:

As stated in the previous office action, applicants claim fluoro replacement for chloro, at the same position. See structures page 6 of office action filed 08/12/2009. Same position but different halogens. To one of skill in the art, halogens (F, Cl, Br, I) are suggestive of one another and are obvious variants, such that no secondary teaching is needed for one of skill in the art to choose over the other.

Rejection over Yamamoto and Bream:

Applicant's arguments center on the following:

1. The same reasoning as recited above in the above rejections
2. The combination still fails to render the claimed subject matter because the presently claimed compounds are significantly different and distinguishable in structure from those disclosed in Yamamoto and Bream and neither Yamamoto and Bream provide motivation and suggestion.

Response:

The combination represents the critical difference between the prior art compounds and the instantly claimed compounds: positional isomers, adjacent homologs, and obvious variants that provide for combination of elements to make alternate forms of known compounds.

Note: Applicants Remarks correspond to the previously presented prior art citations which relate to only few of the over abundance of prior art possibilities available for obviousness rejection.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nizal S Chandrakumar/
Examiner, Art Unit 1625

/D. Margaret Seaman/
Primary Examiner, Art Unit 1625